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**REMARKS**

The final Office Action mailed October 29, 2003 has been received and carefully considered. Initially, Applicants resubmit the references which were originally and properly included with the August 13, 2003 response with a copy of the date-stamped postcard indicating receipt of the references by the USPTO. Therefore, Applicants respectfully request the Examiner to consider the references and indicate his consideration thereof by initialing and returning to Applicants a copy of the Form PTO/SB/08A. No fee is accompanying the Information Disclosure Statement as the fee has previously been paid. Additionally, Applicants believe consideration is appropriate as the references were originally provided prior to a Final Office Action. Should the Examiner have any remaining concerns please feel free to contact the undersigned.

Applicants have amended the claims in a manner which they believe addresses the Examiner's concerns, and provide the following comments. The amended claims find support throughout the application as originally filed, more particularly on page 5, line 33 through page 6 line 3. No new matter is added as a result of the amendments.

Applicants believe the claims as amended and discussion which follows address the Examiner's remaining concerns regarding the 35 U.S.C. § 112, 1<sup>st</sup> and 2<sup>nd</sup> ¶, 35 U.S.C. § 102, and 35 U.S.C. § 103 rejections.

**Rejection Under 35 U.S.C. § 112 ¶ 1**

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Applicants have cancelled claims 47 and 48 and therefore the rejection is respectfully obviated.

**35 U.S.C. § 112 ¶ 2**

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-11, 14-48 were rejected under 35 U.S.C. § 112 ¶ 2 on page 3 of the Office Action as being indefinite. Initially, as stated in the previous Amendment/Response, Applicants have deleted the phrase "in the same determination routine" from claim 1 and therefore the

rejection is moot. As claim 2 was canceled in the previous Amendment/Response and the phrase “substantially” has been deleted from claim 1 the rejection is obviated. Claims 46-48 have been canceled and therefore the rejection is respectfully obviated.

Applicants respectfully request the rejection be withdrawn.

**35 U.S.C. §102(b)**

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in a public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 and dependent claims 3-6, 9, 16-19, 31, 32, 33, 36, 39, 41, 43 and 45 stand rejected under 35 U.S.C. 102(b) as being anticipated by GB 2 214 518. “Anticipation under 35 U.S.C. § 102 requires the disclosure in a single piece of prior art of each and every limitation of a claimed invention.” (*Electro Med. Sys. S.A. v. Cooper Life Sciences*, 32 U.S.P.Q.2d 1017, 1019 (Fed. Cir. 1994)). The claimed invention is directed to a method for the determination of the absolute concentration of sperm cells in a semen sample and the proportion of live sperm cells therein, comprising subjecting the semen sample or a diluted subsample of the semen sample to selective staining and determining the absolute concentration of the sperm cells and the proportion of live sperm cells by means of a detection means responsive to the selective staining, wherein the determination of the absolute concentration of sperm cells and of the proportion of live sperm cells in the semen sample are performed simultaneously.

GB 2 214 518 discloses a method of determining sperm count and/or living sperm count. The method utilizes blank measurements and the steps of staining the sample with propidium iodide and measuring the fluorescence, F1, to provide a measure of dead sperm cells in the sample, and *subsequently* permeabilizing the sample cells by addition of a permeabilizing agent, that kills the cells in the sample, and measuring the intensity F2 to provide a measure of the total number of permeabilized cells which is proportional to the cell count of the sample. (*See*, the Example, pages 7-10).

As described above, the total or absolute concentration of cells and the proportion of live sperm cells can not be obtained simultaneously from the GB 2 214 518 method. The GB 2 214 518 method requires a prerequisite that the determinations are performed subsequently and in the

order described above to yield any useful result.

Applicants respectfully submit that claim 1 and those which depend therefrom are not anticipated by GB 2 214 518. Applicants respectfully traverse the rejection.

**35 U.S.C. §103(a)**

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-11, 13-29, 31-33, 36-39, 41, 43, 44 and 46 were rejected under 35 U.S.C. § 103(a) as being obvious over US 4,559,309 or JP 8-332098 or Live/Dead Viability Kit or Garner et al. or GB 2 214 518 in combination with EP 586 183 or WO 93/16385.

As the Examiner stated, many in the art have shown a direct correlation between sperm concentration and sperm viability with fertility (Page 8, paragraph 4). The claimed invention provides for a simultaneous determination of viability and absolute concentration. It is the simultaneous determination which has not previously been disclosed. Indeed, the claimed invention provides a method which meets the current demand for obtaining a determination of sperm viability and sperm concentration through a simplified method to increase fertility. This results in an important advantage for artificial insemination (AI) stations. The simultaneous determinations save time and effort at the AI stations. The analysis are typically performed on the AI stations themselves and the procedures thus need to be simple, rapid and safe in order to provide both a method suitable to be used on the AI stations and to provide reliable results.

Typically, in cited references, the viability and the concentration of sperm cells are determined in two steps. First, the viability is determined and subsequently the concentration is determined after all sperm cells have been killed, regardless of the employed procedures for determining viability and concentration, cf. e.g. GB 2 214 518, and Evenson et al., J Dairy Sci. (Provided as an attachment).

The reason for this typical procedure is the lability and sensitivity of the live sperm cells. The sperm need to be handled with much care when a viability measurement is performed and the procedures may likely kill many live sperm cells during handling, staining and measuring. Thus, the standard procedure, and state of the art procedure, is as mentioned above, to perform a

viability determination and subsequently perform a concentration determination on killed or permeablized sperm.

Further, the methods suggested in both EP 585 183 and WO 93/16385 were developed for measuring the concentration in a sample of blood, particularly as described in the examples. Thus, even if the Examiner finds the teaching of these two references to be generic teachings disclosing the use of an internal standard to be used in flow cytometry in cell counting methods, the generic teaching does not account for the sensitivity of the live sperm cells. Therefore, one of skill in the art would apply or relate the teaching of both EP 585 183 and WO 93/16385 to dead or killed sperm cells.

Contrary to the art, the Applicants claim absolute concentration and viability may be obtained simultaneously. Any application of EP 585 183 and WO 93/16385 in combination with any of US 4,559,309, JP 8-332098, Live/Dead Sperm Viability Kit, and Garner et al. to utilize a sperm sample for simultaneous determination of absolute concentration and the proportion of live sperm cells would be based purely on hindsight and not on the teaching of the prior art.

The non-obviousness of the claimed invention in view of the cited references alone or in combination is further rebutted by the accompanying Declaration by Preben Christensen and Torben Greve. Aside from a brief discussion of the related art, the declaration also provides an experiment wherein the variance on the determination of the concentration is at least halved demonstrating the more accurate determination using the claimed method compared to those obtainable by prior art methods.

The effect of a halving of the variance is seen in the enclosed graph. In the graph a threshold of 12 mill sperm/dose is marked and the goal is to obtain sperm doses wherein less than 2.5 % of the doses comprises less sperm than the threshold sperm of 12 mill.

In experiments, sperm concentration has been determined by the use of prior art methods to be a standard deviation of 3 mill sperm/dose whereas the variance using the method of the present invention has been found to be 1.5 mill sperm/dose. Thus, to fulfill the above-mentioned condition of having less than 2.5 % of the doses comprising less than 12 mill sperm, the concentration of each sperm dose has to be centered at 18 mill sperm/dose when determined by traditional methods, whereas the concentration may be centered at 15 mill sperm/dose when the concentration is determined by the method of the present invention. Thus, by using the concentration determination of the present invention, 20 % more doses may be obtained than

when traditional methods are used.

Sperm from boars, bulls, etc. are highly valued articles of commerce and doses from a good and well-reputed breeding bull or boar may be priced from \$50 - \$300, so that a 20 % increase in doses may correspond to a significant revenue for an AI station.

The simultaneous determination of viability provides for example the possibility of rejecting sperm having a viability below a threshold viability and thus presumably increasing the chances of fertilization.

Initially, Applicants respectfully point out that there is no motivation found in any of these references to combine them. Further, prior art references in combination do not make an invention obvious unless something in the prior references would suggest the advantage to be derived from combining their teachings. *In re Sernaker*, 217 U.S.P.Q. 1, 6 (Fed. Cir. 1983). A combination may be patentable whether it be composed of elements all new, partly new or all old. *Rosemont, Inc. v. Beckman Instruments, Inc.*, 221 U.S.P.Q. 1, 7 (Fed. Cir. 1984). There must be something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination. *Lindemann v. Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 221 U.S.P.Q. 481, 488 (Fed. Cir. 1984). *Interconnect Planning Corporation v. Feil, et al.*, 227 U.S.P.Q. 543, 551 (Fed. Cir. 1985). In the present case there is no such motivation. This is particularly true given that none of the references cited by the Examiner recognized that by a simultaneous determination of the total sperm concentration and the number of living sperm cells, the variation may be reduced so that a higher precision is obtained.

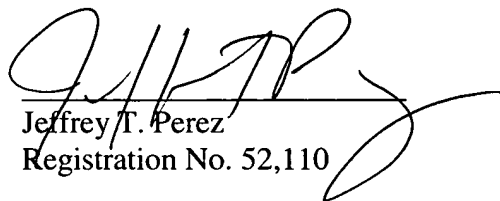
The rejection is respectfully traversed.

**CONCLUSION**

Applicants assert that the above-referenced application is in condition for allowance. Reconsideration and allowance of all pending claims is respectfully requested. Should any outstanding issues remain, the Examiner is invited to telephone the undersigned at 202-955-1500.

Respectfully submitted,

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Dated: 27 Feb 2004



UTILITY ☒

DESIGN ☐

Application Serial No.: 09/914,765

Client/Matter: 60123.000002

Inventor: Preben CHRISTENSEN et al.

Client: De Danske Kvaegalsforeninger

Filing Date: September 5, 2001

Atty/Sec.: SA/JP/jt

Date: August 13, 2003

Title: DETERMINATION OF SPERM CONCENTRATION AND VIABILITY FOR ARTIFICIAL INSEMINATION

The following has been received in the U.S. Patent and Trademark Office on the date stamped hereon:

1. Fee Transmittal for Amendment
2. Request for 3-month Extension of Time
3. Amendment/Response Under 37 CFR 1.111
4. Supplemental IDS
5. SB/08A form (listing 34 documents, all included)
6. Check # 2057343 for \$180
7. Check # 2057342 for \$1032



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